=> d ibib abs hitstr 1-6

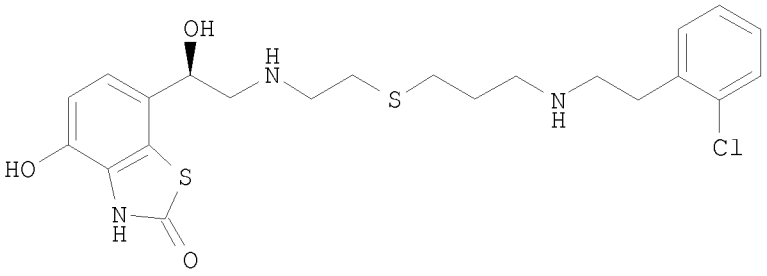
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:1073175 CAPLUS
DOCUMENT NUMBER: 149:332322
TITLE: Preparation of benzothiazolone derivatives for use as beta-2-adrenoceptor agonists
INVENTOR(S): Cadogan, Elaine Bridget; Connolly, Stephen; Nicholls, David John; Young, Alan
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 65pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008104776	A1	20080904	WO 2008-GB667	20080229

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2007-3999 A 20070301
GI



I

AB Title compound I, and its pharmaceutically acceptable salts, are prepared and disclosed as β2-adrenoceptor agonists. Thus, e.g., I•2HBr was prepared by amidation of 2-(2-chlorophenyl)ethanamine with acryloyl chloride followed by thioesterification with Et mercaptoacetate, reduction, N-protection, oxidation, reductive amination with 7-[(1R)-2-amino-1-hydroxyethyl]-4-hydroxy-1,3-benzothiazol-2(3H)-one acetate, and deprotection. I•2HBr was evaluated in various assays including dopamine D2 assays (biodata given).

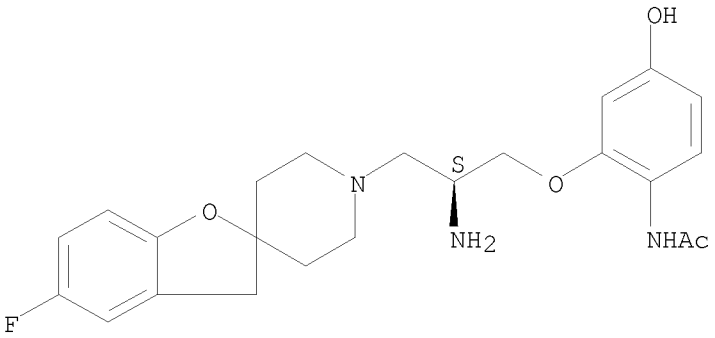
IT 857264-46-1 1053240-20-2 1053240-21-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(co-drug; preparation of benzothiazolone derivs. for use as beta-2-adrenoceptor agonists)

RN 857264-46-1 CAPLUS

CN Acetamide, N-[2-[(2S)-2-amino-3-(5-fluorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-hydroxyphenyl]- (CA INDEX NAME)

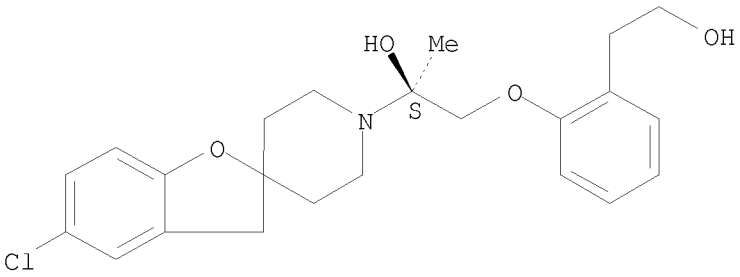
Absolute stereochemistry.



RN 1053240-20-2 CAPLUS

CN Spiro[benzofuran-2(3H),4'-piperidine]-1'-methanol, 5-chloro-α-[[2-(2-hydroxyethyl)phenoxy]methyl]-α-methyl-, (αS)- (CA INDEX NAME)

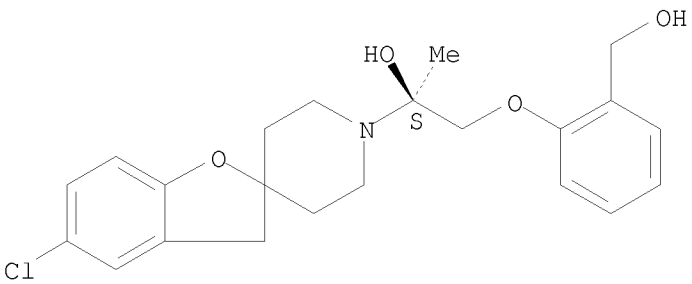
Absolute stereochemistry.



RN 1053240-21-3 CAPLUS

CN Spiro[benzofuran-2(3H),4'-piperidine]-1'-methanol, 5-chloro-α-[[2-(hydroxymethyl)phenoxy]methyl]-α-methyl-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:1045246 CAPLUS
DOCUMENT NUMBER: 149:307681
TITLE: Novel combination of compounds to be used in the treatment of airway diseases, especially chronic obstructive pulmonary disease (COPD) and asthma
INVENTOR(S): Eriksson, Tomas; Hansson, Johan; Mensonides-Harsema, Marguerite; Mo, John
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 81pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008103125	A1	20080828	WO 2008-SE50203	20080221
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2007-891245P P 20070223
OTHER SOURCE(S): MARPAT 149:307681
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to a combination of (a) a chemokine receptor 1 (CCR1) antagonist and (b) a muscarinic antagonist. The CCR1 antagonists are represented by 3-(4-piperidinylamino)-3-phenoxypropan-2-ol derivs. [I; m = 0-2; R1 = halogen, C1-3 haloalkyl, cyano; X1 = CH2 or C(O); n, p = 0-2; R2 = C1-6 cycloalkyl; or R2 forms a bicyclic ring together with the ring it is attached to; R3 = H, C1-4 alkyl; R4 = H, halo, HO, (un)substituted C1-6 hydroxyalkyl; A = a bond or C1-6 haloalkyl; R5 = H, HO, NHC(O)R6, NHS(O)2R6, (un)substituted CONH2, CO2R9, or SO3R9; R6 = H, C1-6 alkyl or (un)substituted 3 to 6-membered saturated or unsatd. ring, optionally comprising one or more heteroatom selected from N, O, and S; R9 = H, C1-6 alkyl; q = 0-2; R10 = halogen, HO, cyano, C1-3 haloalkyl or C1-6 alkoxy] or benzene-fused spiropyrrolidine or spiropiperidine compds. [II; r, s = 0-2; R11 = halogen, cyano, C1-6 haloalkyl; X, Y, Z = a bond, O, NH, CH2, C(O); R12 = C1-6 cycloalkyl; u = 0-1; R21 = H, HO, NH2; R13 is hydrogen or C1-6alkyl; A1 = a bond, C1-3alkyl; R15 = H, HO, NHC(O)R16, -NHS(O)2R16, (un)substituted CONH2, CO2R19, SO3R19; R14 = H, halo, HO, OC(CH3)2CO2H, (un)substituted C1-6 hydroxyalkyl; t = 0-2; R16 = H, C1-3

alkyl, (un)substituted NH2 or OR19; R19 = H, C1-3 alkyl; R20 = halo, cyano, C1-3 alkoxy or C1-3 haloalkyl] or pharmaceutically acceptable salts thereof. The invention further relates to pharmaceutical compns. comprising said combination and to methods of treatment of airway diseases, such as chronic obstructive pulmonary disease (COPD) and asthma in mammals by administering said combination. The invention further relates to a kit comprising the combination and use of said kit in treatment of airway diseases. A combination of a CCR1 antagonist with a muscarinic antagonist is considered to be particularly effective in reducing inflammatory cell influx into the lung. The beneficial effect may be observed when the two active substances are administered simultaneously (either in a single pharmaceutical composition or in sep. compns.), or sequentially or sep. Thus, a solution of N-ethyl-N'-[2-((2S)-oxiran-2-ylmethoxy)phenyl]urea and 1-(4-chlorobenzyl)piperidin-4-amine in EtOH was heated to 80° for 12 h to give N-[2-[[(2S)-3-[[1-(4-chlorobenzyl)-4-piperidinyl]amino]-2-hydroxypropyl]oxy]phenyl]-N'-ethylurea (III). A combination of 2-[2-chloro-5-[[(2S)-3-(5-chloro-2,3-dihydrospiro[benzofuran-2,4'-piperidin]-1'-yl)-2-hydroxypropyl]oxy]-4-[(methylamino)carbonyl]phenoxy]-2-methylpropanoic acid (IV) and tiotropium significantly decreased a total and neutrophil cell number in bronchoalveolar lavage (BAL) fluid of rats challenged intratracheally (i.t.) with lipopolysaccharide compared to the group administered with IV or tiotropium alone.

IT 857264-47-2P, N-[2-[[(2S)-2-Amino-3-(5-fluoro-2,3-dihydrospiro[benzofuran-2,4'-piperidin]-1'-yl)propyl]oxy]-4-hydroxyphenyl]acetamide bis(trifluoroacetate)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (piperidinylamino)phenoxypropanols or benzene-fused spiropyrrolidines or spiropiperidines for combination therapy of airway diseases)

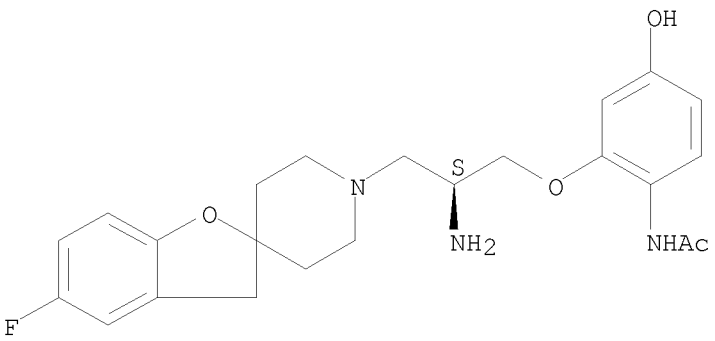
RN 857264-47-2 CAPLUS

CN Acetamide, N-[2-[(2S)-2-amino-3-(5-fluorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-hydroxyphenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

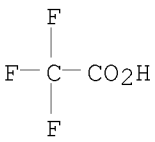
CRN 857264-46-1
CMF C23 H28 F N3 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:1043225 CAPLUS
DOCUMENT NUMBER: 149:307691
TITLE: Novel combination of spiroheterocyclicpiperidines to be used in the treatment of airway diseases, especially chronic obstructive pulmonary disease (copd) and asthma
INVENTOR(S): Eriksson, Tomas; Hansson, Johan; Mensonides-Harsema, Marguerite; Mo, John
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008103126	A1	20080828	WO 2008-SE50204	20080221

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2007-891244P P 20070223
OTHER SOURCE(S): MARPAT 149:307691
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides a pharmaceutical product comprising, in combination of, (a) a (therapeutically effective) dose of a first active ingredient, which is a compound of formula I [m = 0-2; n = 0-2; q = 0 or 1; p = 0-2; R1 = halo, CN, haloalkyl; R2 = (=O) or alkyl; R3 = H, OH, or NH2;

R4 = H, OH, oxo, etc.; R5 = H, halo, OH, (un)substituted alkoxy; A = bond or alkyl; R8 = H or alkyl; R9 = halo, CN, alkoxy, or haloalkyl; X, Y and Z independently = bond, O, NH, CH2 or C(O), provided that only one of X, Y and Z is a bond, and provided that X and Y are not simultaneously O or C(O)] or a pharmaceutically acceptable salt thereof; and (b) a (therapeutically effective) dose of a second active ingredient, which is a glucocorticoid receptor agonist; and optionally, (c) a (therapeutically effective) dose of a third active ingredient, which is a β2-agonist. The invention further relates to pharmaceutical compns. comprising said combination and to methods of treating treatment of airway diseases, especially chronic obstructive pulmonary disease (COPD) and asthma in mammals by administrating said combination. Select I are prepared, e.g., II·TFA was prepared via Wittig reaction of 4-fluoro-2-hydroxybenzaldehyde with Me (triphenylphosphoranylidene)acetate followed by hydrogenation, reaction with (2S)-oxiran-2-ylmethyl 3-nitrobenzenesulfonate, and hydrolysis and workup with TFA. Bioassays are described (no data). The invention further relates to a kit comprising the combination and use of said kit in treatment of airway diseases such as COPD and asthma.

IT 857264-47-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel combination of spiroheterocyclicpiperidines to be used in the treatment of airway diseases, especially chronic obstructive pulmonary disease and asthma)

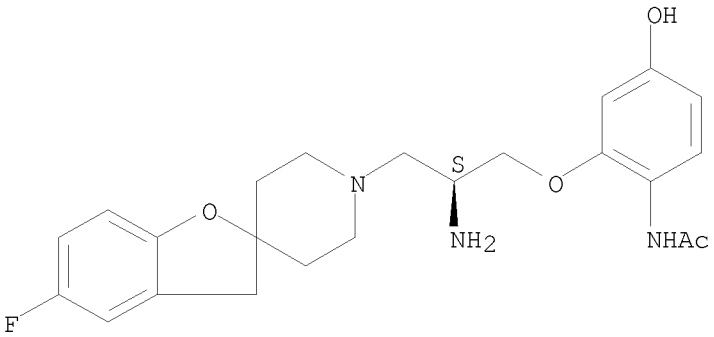
RN 857264-47-2 CAPLUS

CN Acetamide, N-[2-[(2S)-2-amino-3-(5-fluorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-hydroxyphenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

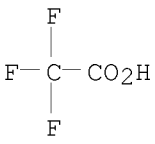
CRN 857264-46-1
CMF C23 H28 F N3 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:15873 CAPLUS
DOCUMENT NUMBER: 144:108216
TITLE: Preparation of amido compounds as inhibitors of 11-β-hydroxysteroid dehydrogenase type 1 (11βHSD1) and antagonists of the mineralocorticoid receptor (MR)
INVENTOR(S): Yao, Wenqing; Xu, Meizhong; Zhang, Colin; Agrios, Konstantinos; Metcalf, Brian; Zhuo, Jincong
PATENT ASSIGNEE(S): Incyte Corporation, USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006002349	A1	20060105	WO 2005-US22411	20050623
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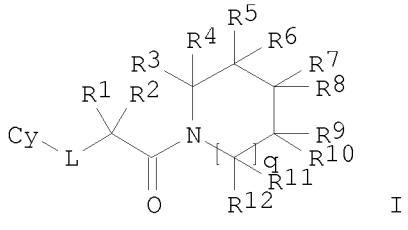
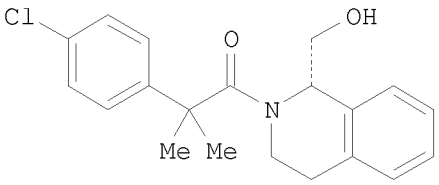
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005258248	A1	20060105	AU 2005-258248	20050623
CA 2571258	A1	20060105	CA 2005-2571258	20050623
US 20060009471	A1	20060112	US 2005-159724	20050623
EP 1758582	A1	20070307	EP 2005-762543	20050623
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1988908	A	20070627	CN 2005-80020965	20050623
JP 2008504278	T	20080214	JP 2007-518299	20050623
BR 2005012410	A	20080304	BR 2005-12410	20050623
IN 2006KN03601	A	20070615	IN 2006-KN3601	20061201
MX 2006PA14572	A	20070312	MX 2006-PA14572	20061213
KR 2007024639	A	20070302	KR 2006-727142	20061222
NO 2007000372	A	20070308	NO 2007-372	20070119

PRIORITY APPLN. INFO.:	US 2004-582556P	P	20040624
	US 2004-639179P	P	20041222
	WO 2005-US22411	W	20050623

OTHER SOURCE(S): CASREACT 144:108216; MARPAT 144:108216
GI



I



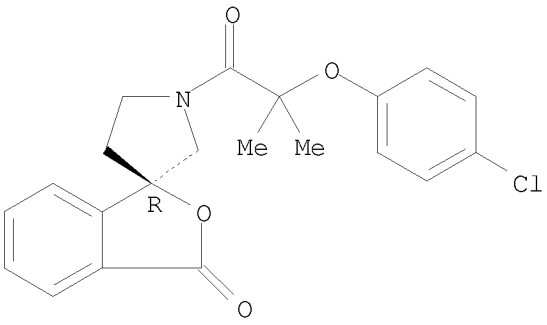
II

AB The title compds. I [Cy = (un)substituted (hetero)aryl, (hetero)cycloalkyl; L = absent, (CR13R14)m, (CR13R14)nO(CR13R14)p, etc.; R1, R2 = (un)substituted alkyl; R3-R12 = H, W1X1Y1Z1; or R3 and R4 together or R5 and R6 together or R7 and R8 together or R9 and R10 together or R11 and R12 together form 4-20 membered cycloalkyl or (un)substituted heterocycloalkyl; or R3 and R12 together or R3 and R10 together or R3 and R8 together or R5 and R10 together or R5 and R10 together or R7 and R12 together form (un)substituted alkylene bridge; R13, R14 = H, halo, alkyl, etc.; W1 = absent, alkylenyl, O, etc.; X1 = absent, alkylenyl, aryl, etc.; Y1 = absent, O, S, etc.; Z1 = H, halo, CN, etc.; m = 1-4; n = 0-3; p = 0-3; q = 0-2; with the provisos] which are inhibitors of 11-β hydroxysteroid dehydrogenase type 1 and antagonists of the mineralocorticoid receptor (MR), were prepared Thus, reacting 2-(4-chlorophenyl)-2-methylpropanoic acid with (1S)-1,2,3,4-tetrahydroisoquinolin-1-ylmethanol in the presence of BOP and N-methylmorpholine in DMF afforded (1S)-II. The compds. I can be useful in the treatment of various diseases associated with expression or activity of 11-β hydroxysteroid dehydrogenase type 1 and/or diseases associated with aldosterone excess. The pharmaceutical composition comprising the compound I is disclosed.

IT 872985-55-2P 872986-34-0P 872986-36-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of amido compds. as inhibitors of 11-β-hydroxysteroid dehydrogenase type 1 (11βHSD1) and antagonists of the mineralocorticoid receptor (MR))

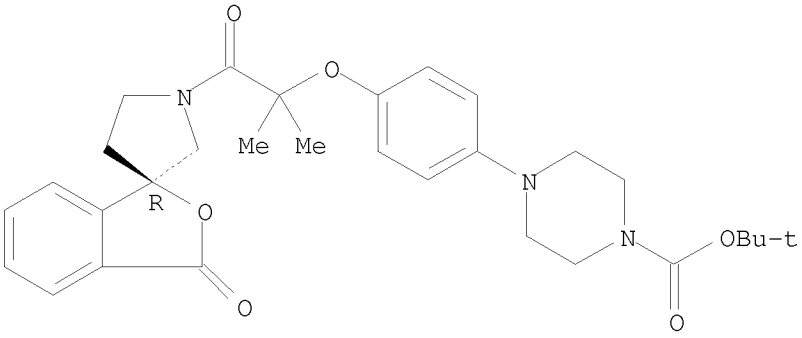
RN 872985-55-2 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one, 1'-[2-(4-chlorophenoxy)-2-methyl-1-oxopropyl]-, (1R)- (CA INDEX NAME)

Absolute stereochemistry.



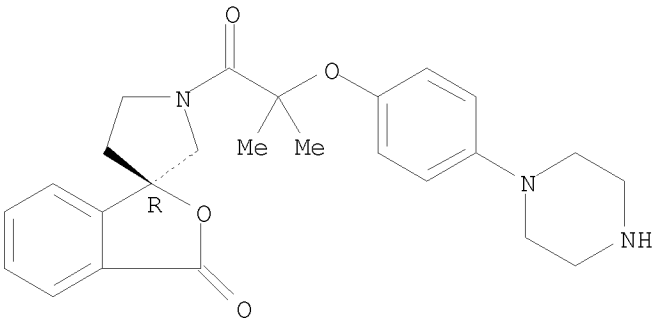
RN 872986-34-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[1,1-dimethyl-2-oxo-2-[(1R)-3-oxospiro[isobenzofuran-1(3H),3'-pyrrolidin]-1'-yl]ethoxy]phenyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



RN 872986-36-2 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one, 1'-[2-methyl-1-oxo-2-[4-(1-piperazinyl)phenoxy]propyl]-, (1R)- (CA INDEX NAME)

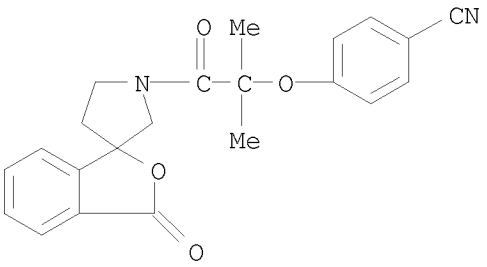
Absolute stereochemistry.



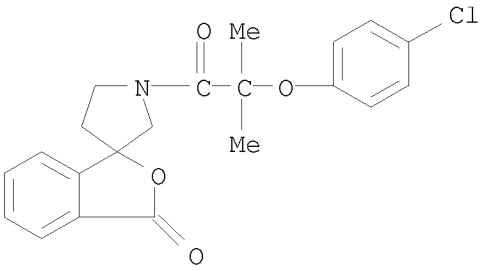
IT 872985-48-3P 872985-49-4P 872985-50-7P
872985-51-8P 872985-52-9P 872985-53-0P
872985-54-1P 872985-56-3P 872985-57-4P
872986-15-7P 872986-19-1P 872986-21-5P
872986-23-7P 872986-25-9P 872986-27-1P

872986-38-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amido compds. as inhibitors of 11-β-hydroxysteroid dehydrogenase type 1 (11βHSD1) and antagonists of the mineralocorticoid receptor (MR))

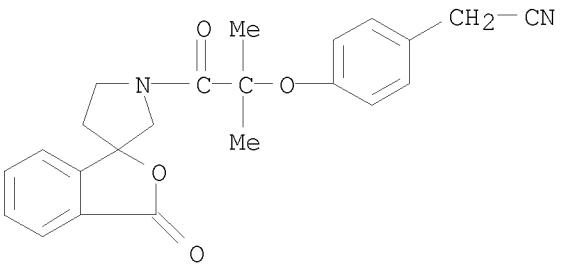
RN 872985-48-3 CAPLUS
CN Benzonitrile, 4-[1,1-dimethyl-2-oxo-2-(3-oxospiro[isobenzofuran-1(3H),3'-pyrrolidin]-1'-yl)ethoxy]- (CA INDEX NAME)



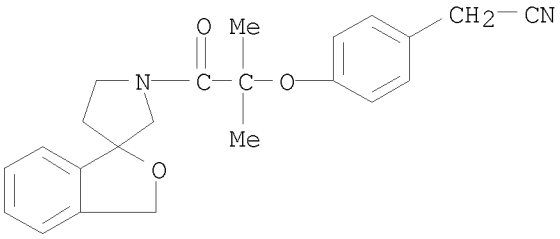
RN 872985-49-4 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one, 1'-[2-(4-chlorophenoxy)-2-methyl-1-oxopropyl]- (CA INDEX NAME)



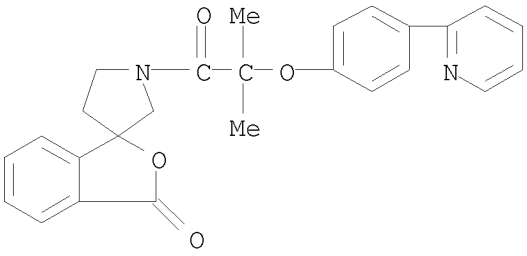
RN 872985-50-7 CAPLUS
CN Benzeneacetonitrile, 4-[1,1-dimethyl-2-oxo-2-(3-oxospiro[isobenzofuran-1(3H),3'-pyrrolidin]-1'-yl)ethoxy]- (CA INDEX NAME)



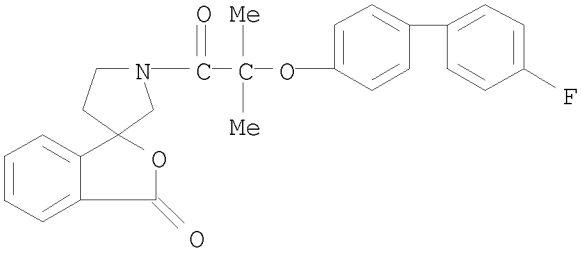
RN 872985-51-8 CAPLUS
CN Benzeneacetonitrile, 4-[1,1-dimethyl-2-oxo-2-(spiro[isobenzofuran-1(3H),3'-pyrrolidin]-1'-yl)ethoxy]- (CA INDEX NAME)



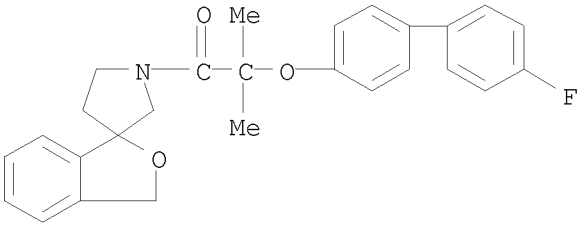
RN 872985-52-9 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one, 1'-[2-methyl-1-oxo-2-[4-(2-pyridinyl)phenoxy]propyl]- (CA INDEX NAME)



RN 872985-53-0 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one, 1'-[2-[(4'-fluoro[1,1'-biphenyl]-4-yl)oxy]-2-methyl-1-oxopropyl]- (CA INDEX NAME)



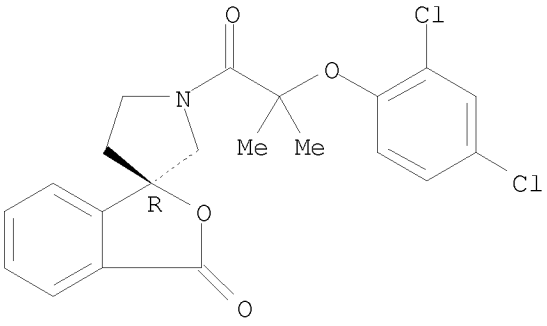
RN 872985-54-1 CAPLUS
CN 1-Propanone, 2-[(4'-fluoro[1,1'-biphenyl]-4-yl)oxy]-2-methyl-1-(spiro[isobenzofuran-1(3H),3'-pyrrolidin]-1'-yl)- (CA INDEX NAME)



RN 872985-56-3 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one,

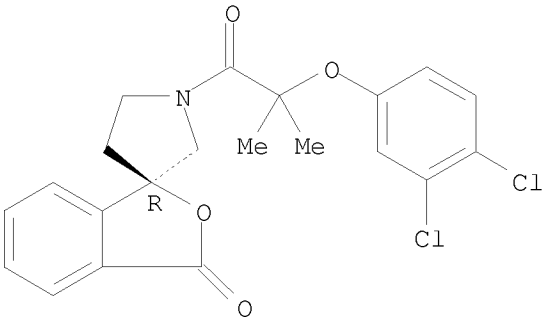
1'-[2-(2,4-dichlorophenoxy)-2-methyl-1-oxopropyl]-, (1R)- (CA INDEX NAME)

Absolute stereochemistry.



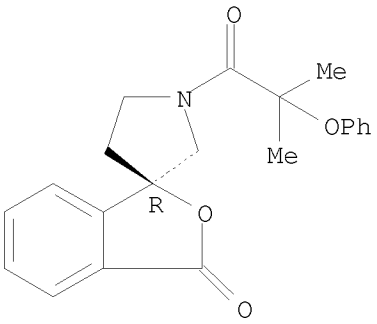
RN 872985-57-4 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one,
1'-[2-(3,4-dichlorophenoxy)-2-methyl-1-oxopropyl]-, (1R)- (CA INDEX NAME)

Absolute stereochemistry.



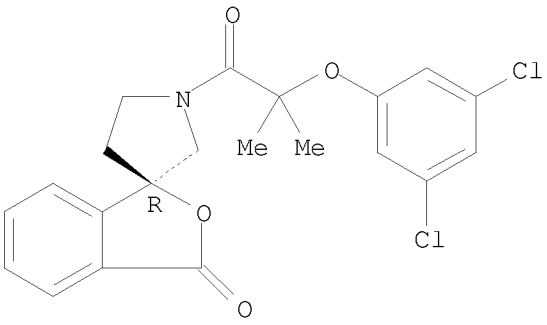
RN 872986-15-7 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one,
1'-(2-methyl-1-oxo-2-phenoxypropyl)-, (1R)- (CA INDEX NAME)

Absolute stereochemistry.



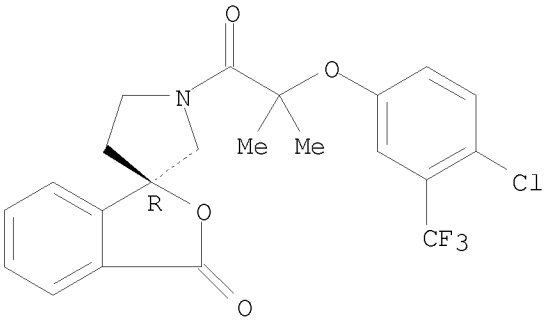
RN 872986-19-1 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one,
1'-[2-(3,5-dichlorophenoxy)-2-methyl-1-oxopropyl]-, (1R)- (CA INDEX NAME)

Absolute stereochemistry.



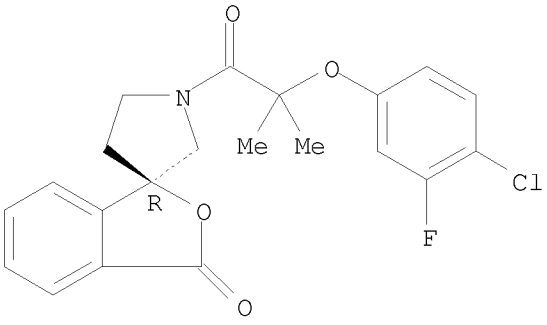
RN 872986-21-5 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one, 1'-[2-[4-chloro-3-(trifluoromethyl)phenoxy]-2-methyl-1-oxopropyl]-, (1R)- (CA INDEX NAME)

Absolute stereochemistry.



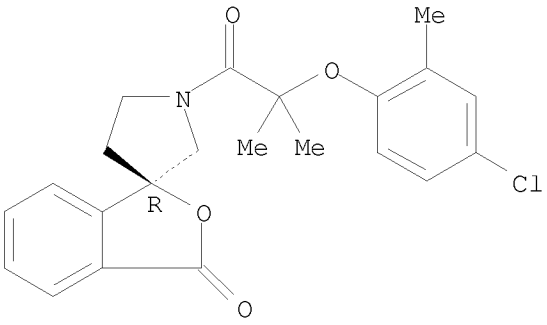
RN 872986-23-7 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one, 1'-[2-(4-chloro-3-fluorophenoxy)-2-methyl-1-oxopropyl]-, (1R)- (CA INDEX NAME)

Absolute stereochemistry.



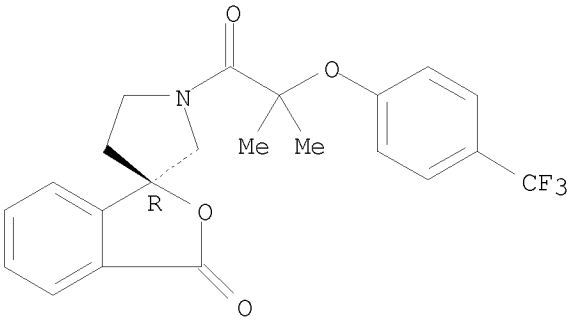
RN 872986-25-9 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one, 1'-[2-(4-chloro-2-methylphenoxy)-2-methyl-1-oxopropyl]-, (1R)- (CA INDEX NAME)

Absolute stereochemistry.



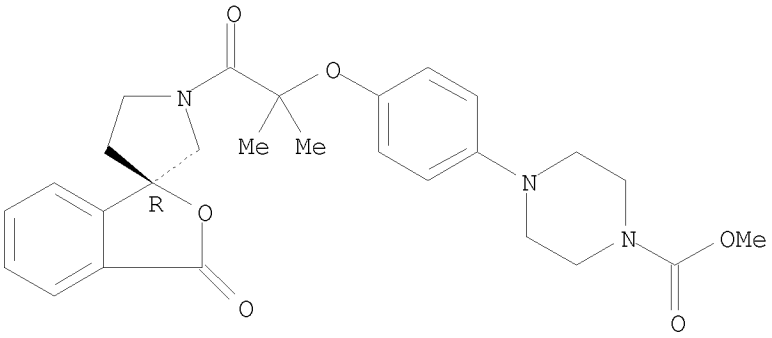
RN 872986-27-1 CAPLUS
CN Spiro[isobenzofuran-1(3H),3'-pyrrolidin]-3-one, 1'-[2-methyl-1-oxo-2-[4-(trifluoromethyl)phenoxy]propyl]-, (1R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 872986-38-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[1,1-dimethyl-2-oxo-2-[(1R)-3-oxospiro[isobenzofuran-1(3H),3'-pyrrolidin]-1'-yl]ethoxy]phenyl]-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



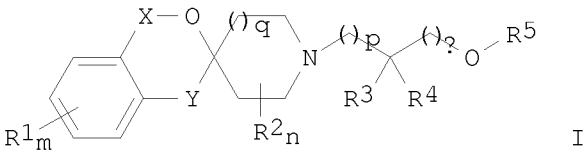
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:588965 CAPLUS

DOCUMENT NUMBER: 143:115452
TITLE: Preparation of tricyclic spiropiperidines as modulators of chemokine receptor activity
INVENTOR(S): Hossain, Nafizal; Ivanova, Svetlana
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005061499	A1	20050707	WO 2004-SE1938	20041220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004303735	A1	20050707	AU 2004-303735	20041220
AU 2004303735	B2	20070920		
CA 2548494	A1	20050707	CA 2004-2548494	20041220
EP 1699791	A1	20060913	EP 2004-809111	20041220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS				
BR 2004017036	A	20070206	BR 2004-17036	20041220
CN 1918160	A	20070221	CN 2004-80042013	20041220
JP 2007515476	T	20070614	JP 2006-546906	20041220
MX 2006PA07025	A	20060831	MX 2006-PA7025	20060619
US 20070099945	A1	20070503	US 2006-583468	20060620
IN 2006MN00848	A	20070518	IN 2006-MN848	20060718
NO 2006003355	A	20060922	NO 2006-3355	20060719
PRIORITY APPLN. INFO.:			SE 2003-3541 A	20031222
			WO 2004-SE1938 W	20041220

OTHER SOURCE(S): CASREACT 143:115452; MARPAT 143:115452
GI



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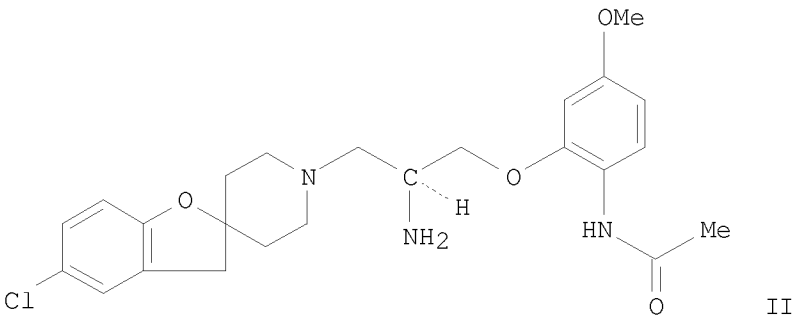


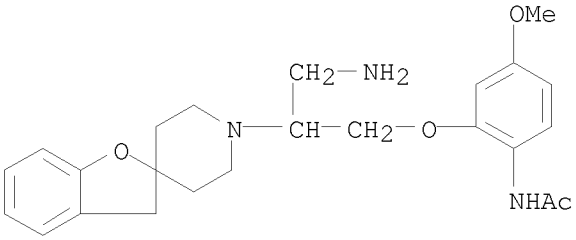
II

AB Title compds. I [m = 0-4; R1 = halo, CN, OH, etc.; X = bond, CH2 and Y = bond, CH2 provided that X, Y do not both simultaneously represent bond, CH2; n = 0-2; R2 = halo, alkyl, haloalkyl; q = 0-1; p = 0-2; R3 = halo, amino, carboxyl, etc.; R4 = H, alkyl, haloalkyl, halo; a = 0-2 provided that p and a are not both 0; R5 = (un)saturated 5-10-membered ring system] are prepared For instance, II is prepared in 4 steps from 5-methoxy-2-nitrophenol, (S)-oxiran-2-ylmethanol, and 5-chlorospiro[3H-benzofuran-2,4'-piperidine] (preparation given). I are modulators of chemokine receptor activity [no data] and useful for the treatment of, e.g., rheumatoid arthritis.

IT 857264-51-8P, N-[2-[3-Amino-2-(spiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]acetamide
RL: BYP (Byproduct); PREP (Preparation)
(preparation of tricyclic spiropiperidines as modulators of chemokine receptor activity)

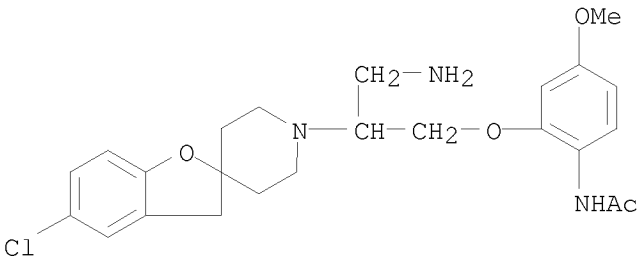
RN 857264-51-8 CAPLUS

CN Acetamide, N-[2-[3-amino-2-(spiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]- (CA INDEX NAME)



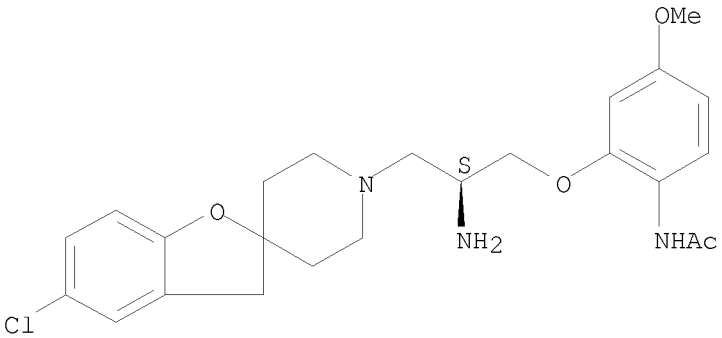
IT 857264-43-8P, N-[2-[[3-Amino-2-(5-chlorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propyl]oxy]-4-methoxyphenyl]acetamide
RL: BYP (Byproduct); SPN (Synthetic preparation); PREP (Preparation)
(preparation of tricyclic spiropiperidines as modulators of chemokine receptor activity)

RN 857264-43-8 CAPLUS
CN Acetamide, N-[2-[3-amino-2-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]- (CA INDEX NAME)



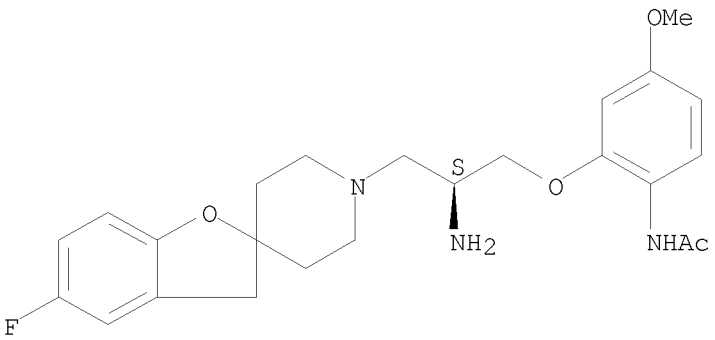
IT 857264-40-5P, N-[2-[[(2S)-2-Amino-3-(5-chlorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propyl]oxy]-4-methoxyphenyl]acetamide
857264-44-9P, N-[2-[[(2S)-2-Amino-3-(5-fluorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propyl]oxy]-4-methoxyphenyl]acetamide
857264-48-3P, N-[2-[[(2S)-2-Amino-3-(spiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propyl]oxy]-4-methoxyphenyl]acetamide
857264-70-1P, 5-[[(2S)-2-Amino-3-(5-fluorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propyl]oxy]-2H-1,4-benzoxazin-3(4H)-one
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of tricyclic spiropiperidines as modulators of chemokine receptor activity)
RN 857264-40-5 CAPLUS
CN Acetamide, N-[2-[(2S)-2-amino-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]- (CA INDEX NAME)

Absolute stereochemistry.



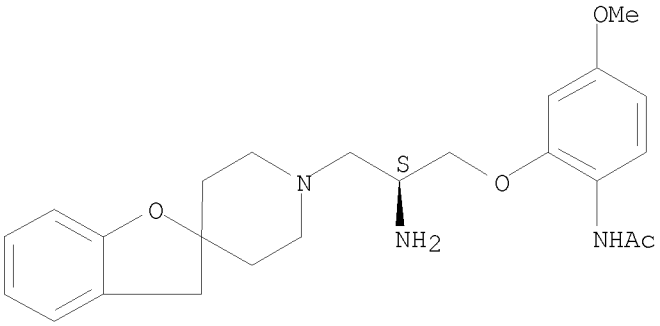
RN 857264-44-9 CAPLUS
CN Acetamide, N-[2-[(2S)-2-amino-3-(5-fluorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]- (CA INDEX NAME)

Absolute stereochemistry.



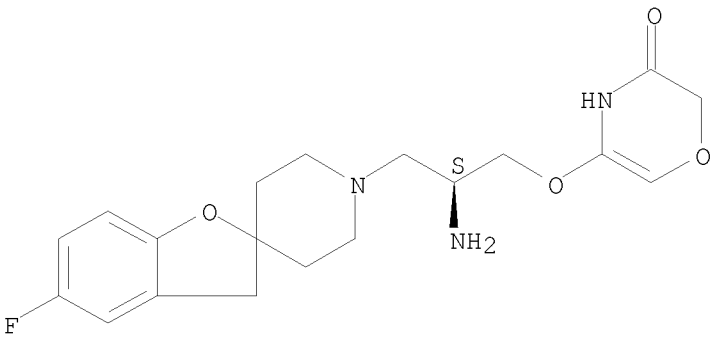
RN 857264-48-3 CAPLUS
CN Acetamide, N-[2-[(2S)-2-amino-3-(spiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 857264-70-1 CAPLUS
CN 2H-1,4-Oxazin-3(4H)-one, 5-[(2S)-2-amino-3-(5-fluorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]- (CA INDEX NAME)

Absolute stereochemistry.



IT 857264-47-2P 857264-53-0P 857264-54-1P,
N-[2-[[(2S)-2-(Acetylamino)-3-(5-fluorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propyl]oxy]-4-methoxyphenyl]acetamide 857264-55-2P
857264-57-4P 857264-58-5P 857264-60-9P
857264-64-3P 857264-67-6P 857264-69-8P

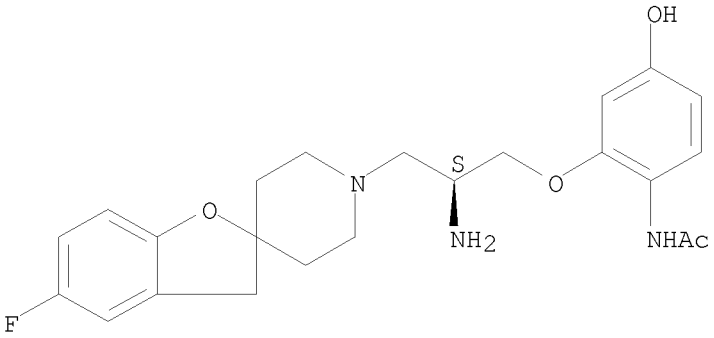
857264-75-6P, 8-[[(2S)-2-Amino-3-(5-fluorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propyl]oxy]quinolin-2(1H)-one 857264-76-7P, 5-Chloro-2-[2-chloro-3-(5-chlorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propoxy]-4-hydroxybenzoic acid 857264-77-8P 857264-80-3P, 2-[2-Amino-3-(5-chlorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propoxy]-5-chloro-4-hydroxybenzoic acid 857264-81-4P 857264-82-5P, 5-Chloro-2-[3-(5-chlorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)-2-(methylamino)propoxy]-4-hydroxybenzoic acid 857264-83-6P 857264-84-7P, 5-Chloro-2-[3-(5-chlorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)-2-(dimethylamino)propoxy]-4-hydroxybenzoic acid 857264-85-8P 857264-87-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tricyclic spiropiperidines as modulators of chemokine receptor activity)

RN 857264-47-2 CAPLUS
CN Acetamide, N-[2-[(2S)-2-amino-3-(5-fluorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-hydroxyphenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

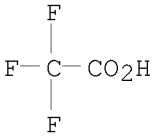
CRN 857264-46-1
CMF C23 H28 F N3 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



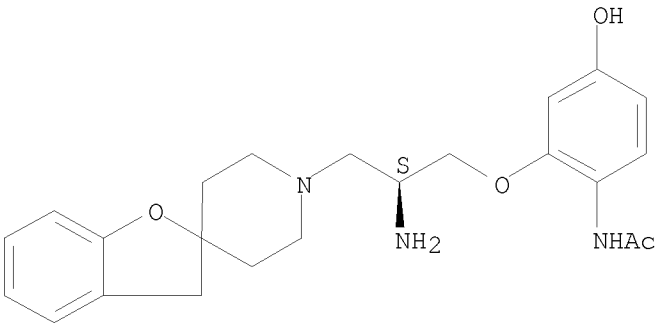
RN 857264-53-0 CAPLUS
CN Acetamide, N-[2-[(2S)-2-amino-3-(spiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-hydroxyphenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX

NAME)

CM 1

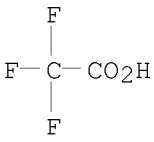
CRN 857264-52-9
CMF C23 H29 N3 O4

Absolute stereochemistry.



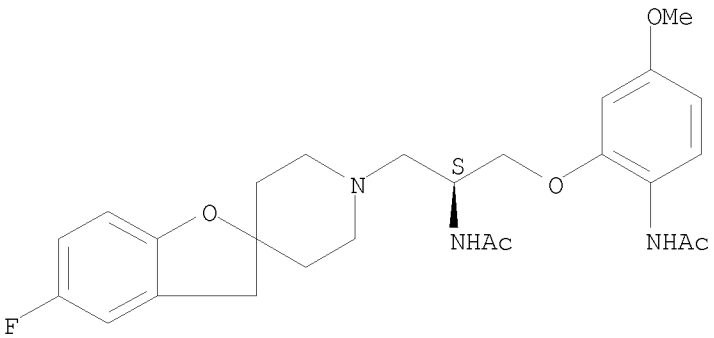
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 857264-54-1 CAPLUS
CN Acetamide, N-[2-[(2S)-2-(acetylamino)-3-(5-fluorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]- (CA INDEX NAME)

Absolute stereochemistry.

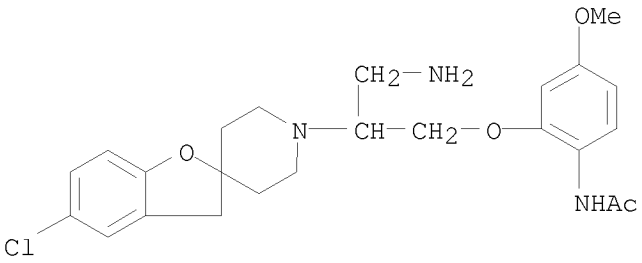


RN 857264-55-2 CAPLUS
CN Acetamide, N-[2-[3-amino-2-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX

NAME)

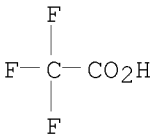
CM 1

CRN 857264-43-8
CMF C24 H30 Cl N3 O4



CM 2

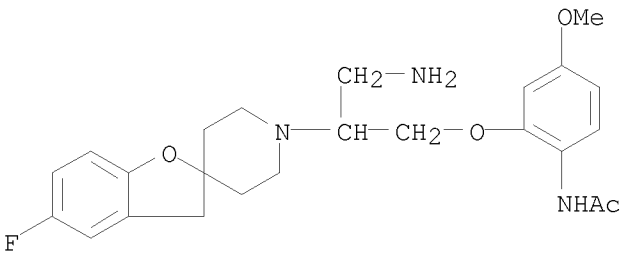
CRN 76-05-1
CMF C2 H F3 O2



RN 857264-57-4 CAPLUS
CN Acetamide, N-[2-[3-amino-2-(5-fluorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

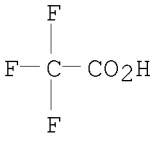
CM 1

CRN 857264-56-3
CMF C24 H30 F N3 O4



CM 2

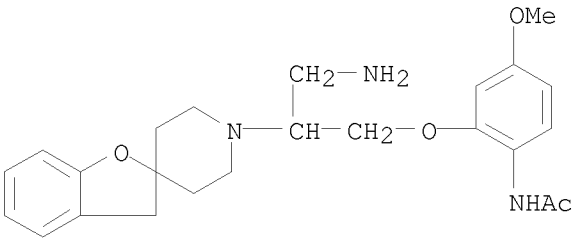
CRN 76-05-1
CMF C2 H F3 O2



RN 857264-58-5 CAPLUS
CN Acetamide, N-[2-[3-amino-2-(spiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

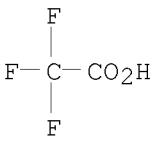
CM 1

CRN 857264-51-8
CMF C24 H31 N3 O4



CM 2

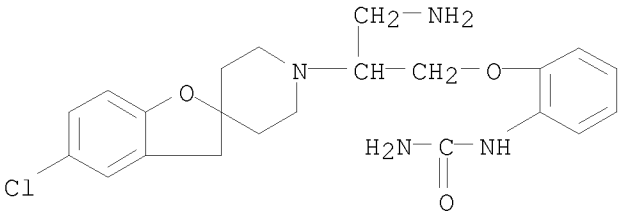
CRN 76-05-1
CMF C2 H F3 O2



RN 857264-60-9 CAPLUS
CN Urea, N-[2-[3-amino-2-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]phenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

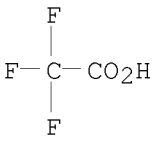
CM 1

CRN 857264-59-6
CMF C22 H27 Cl N4 O3



CM 2

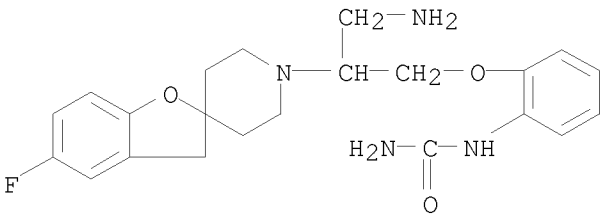
CRN 76-05-1
CMF C2 H F3 O2



RN 857264-64-3 CAPLUS
CN Urea, N-[2-[3-amino-2-(5-fluorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]phenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

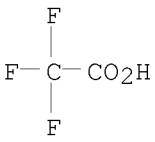
CM 1

CRN 857264-63-2
CMF C22 H27 F N4 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

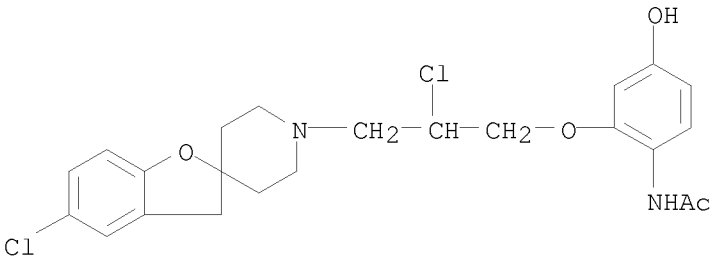


RN 857264-67-6 CAPLUS

CN Acetamide, N-[2-[2-chloro-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-hydroxyphenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

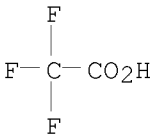
CM 1

CRN 857264-66-5
CMF C23 H26 Cl2 N2 O4



CM 2

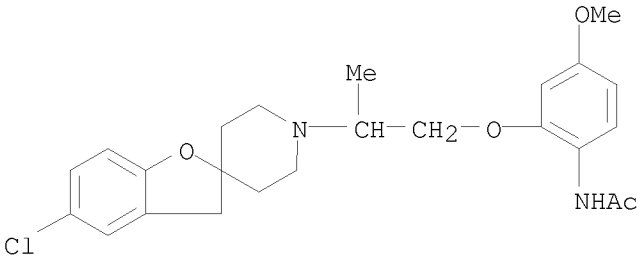
CRN 76-05-1
CMF C2 H F3 O2



RN 857264-69-8 CAPLUS
CN Acetamide, N-[2-[2-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

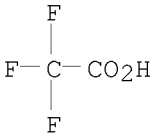
CM 1

CRN 857264-68-7
CMF C24 H29 Cl N2 O4



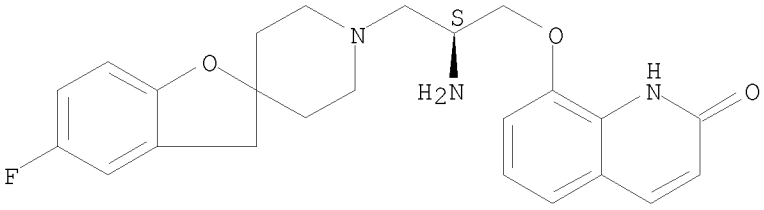
CM 2

CRN 76-05-1
CMF C2 H F3 O2

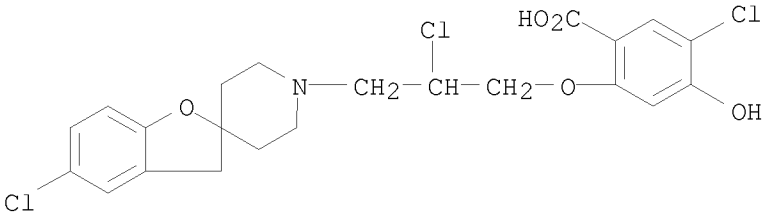


RN 857264-75-6 CAPLUS
CN 2(1H)-Quinolinone, 8-[(2S)-2-amino-3-(5-fluorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]- (CA INDEX NAME)

Absolute stereochemistry.



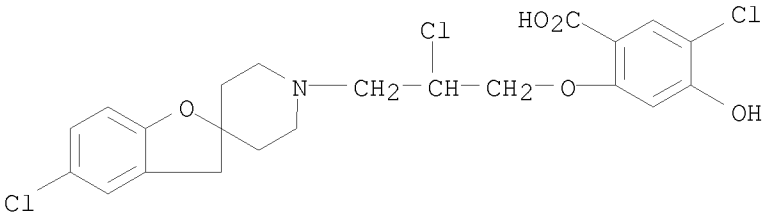
RN 857264-76-7 CAPLUS
CN Benzoic acid, 5-chloro-2-[2-chloro-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-hydroxy- (CA INDEX NAME)



RN 857264-77-8 CAPLUS
CN Benzoic acid, 5-chloro-2-[2-chloro-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

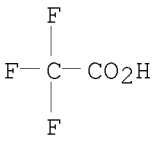
CM 1

CRN 857264-76-7
CMF C22 H22 Cl3 N O5

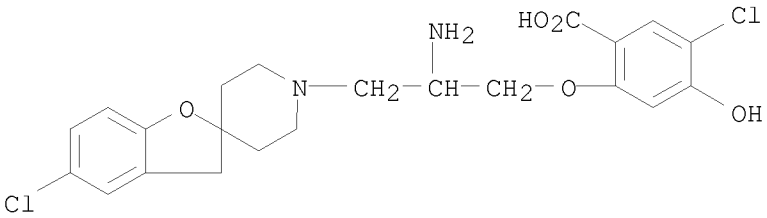


CM 2

CRN 76-05-1
CMF C2 H F3 O2



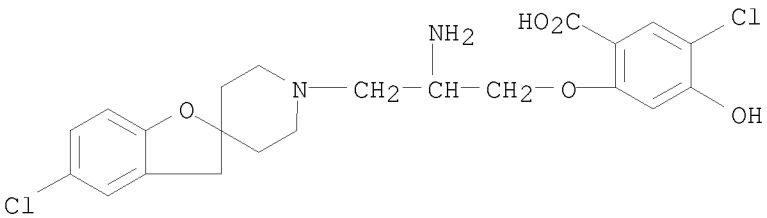
RN 857264-80-3 CAPLUS
CN Benzoic acid, 2-[2-amino-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-5-chloro-4-hydroxy- (CA INDEX NAME)



RN 857264-81-4 CAPLUS
CN Benzoic acid, 2-[2-amino-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-5-chloro-4-hydroxy-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

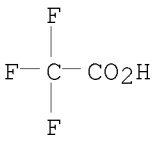
CM 1

CRN 857264-80-3
CMF C22 H24 Cl2 N2 O5

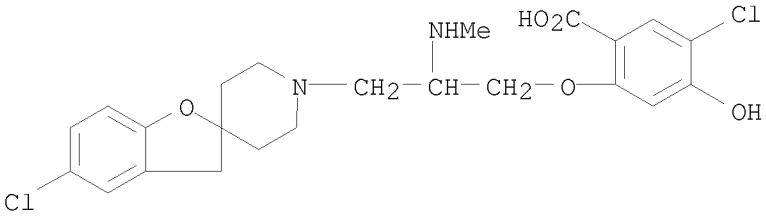


CM 2

CRN 76-05-1
CMF C2 H F3 O2



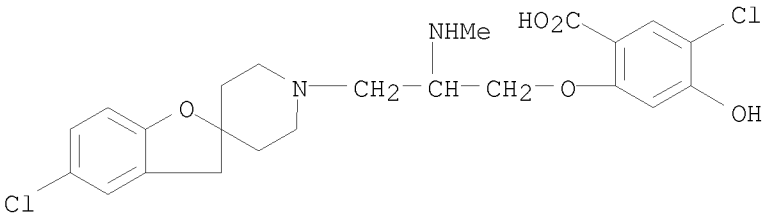
RN 857264-82-5 CAPLUS
CN Benzoic acid, 5-chloro-2-[3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)-2-(methylamino)propoxy]-4-hydroxy- (CA INDEX NAME)



RN 857264-83-6 CAPLUS
CN Benzoic acid, 5-chloro-2-[3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)-2-(methylamino)propoxy]-4-hydroxy-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

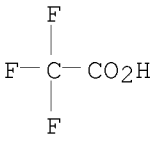
CM 1

CRN 857264-82-5
CMF C23 H26 Cl2 N2 O5

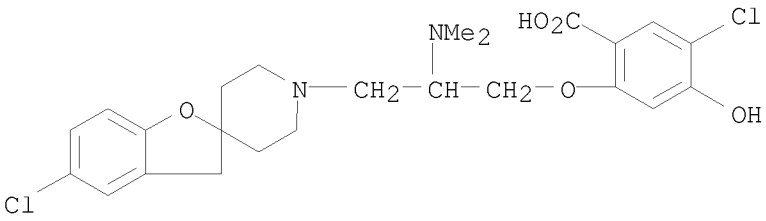


CM 2

CRN 76-05-1
CMF C2 H F3 O2



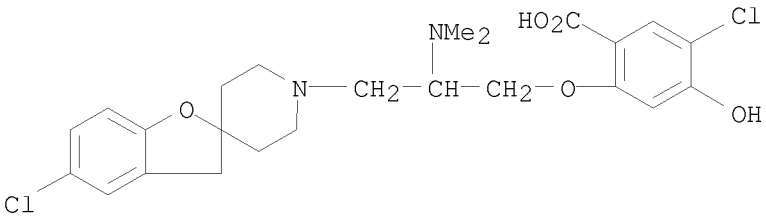
RN 857264-84-7 CAPLUS
CN Benzoic acid, 5-chloro-2-[3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)-2-(dimethylamino)propoxy]-4-hydroxy- (CA INDEX NAME)



RN 857264-85-8 CAPLUS
CN Benzoic acid, 5-chloro-2-[3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)-2-(dimethylamino)propoxy]-4-hydroxy-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

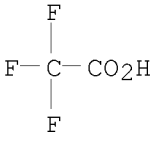
CM 1

CRN 857264-84-7
CMF C24 H28 Cl2 N2 O5



CM 2

CRN 76-05-1
CMF C2 H F3 O2



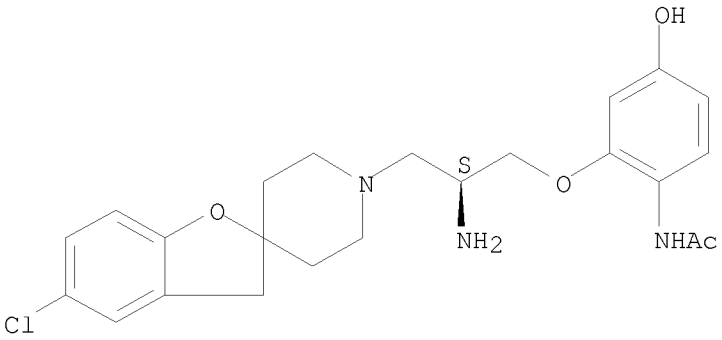
RN 857264-87-0 CAPLUS
CN Acetamide, N-[2-[(2S)-2-amino-3-(5-chlorospiro[benzofuran-2(3H),4'-

piperidin]-1'-yl)propoxy]-4-hydroxyphenyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

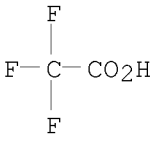
CRN 857264-86-9
CMF C23 H28 Cl N3 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



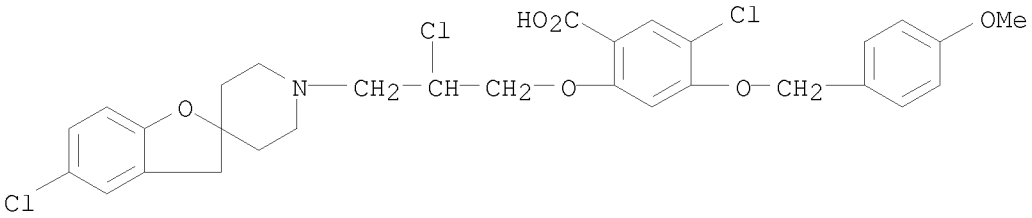
IT 857264-79-0P, 5-Chloro-2-[2-chloro-3-(5-chlorospiro[3H-benzofuran-2,4'-piperidin]-1'-yl)propoxy]-4-[(4-methoxybenzyl)oxy]benzoic acid trifluoroacetate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tricyclic spiropiperidines as modulators of chemokine receptor activity)

RN 857264-79-0 CAPLUS

CN Benzoic acid, 5-chloro-2-[2-chloro-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)propoxy]-4-[(4-methoxyphenyl)methoxy]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

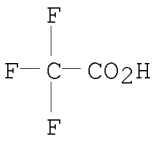
CM 1

CRN 857264-78-9
CMF C30 H30 Cl3 N O6



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:41477 CAPLUS
DOCUMENT NUMBER: 140:93937
TITLE: Preparation of tricyclic spiropiperidines or spiropyrrolidines useful against disorders affected by modulation of chemokine receptors
INVENTOR(S): Hossain, Nafizal; Ivanova, Svetlana; Mensonides-Harsema, Marguerite
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 281 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003243122	A1	20040123	AU 2003-243122	20030707
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EP 1521757	A1	20050413	EP 2003-762957		20030707
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HK 1074622	A1	20080613	HK 2005-106846		20050809
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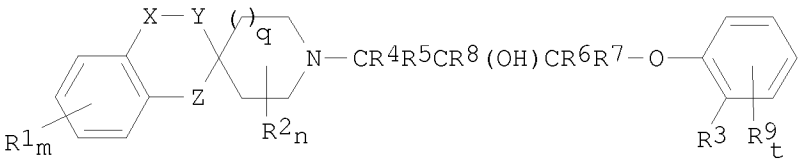
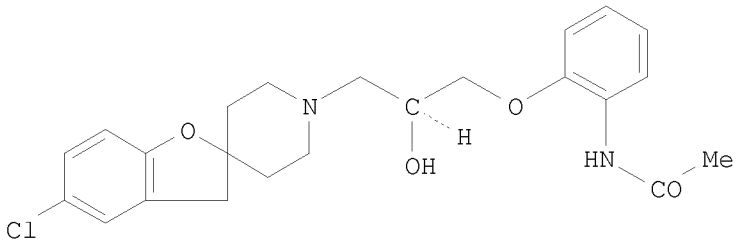
PRIORITY APPLN. INFO.:			SE 2002-2133	A	20020708
			CN 2003-819146	A3	20030707
			WO 2003-SE1185	W	20030707
			IN 2004-DN4014	A3	20041216

OTHER SOURCE(S): MARPAT 140:93937

GI



I



II

AB The invention provides tricyclic spiropiperidines or spiropyrrolidines (shown as I; variables defined below; e.g. II), processes for their preparation, pharmaceutical compns. containing them and their use in therapy for disorders affected by modulation of chemokine receptors (no data). For I: m is 0-4; each R1 = halogen, cyano, hydroxy, C1-C6 alkyl, C1-C6 haloalkyl, C1-C6 alkoxy or sulfonamido; either X = a bond, -CH2-, -O- or -C(O)- and Y = a bond, -CH2-, -O- or -C(O)-, or X and Y together = -CH:CMe- or -CMe:CH-, and Z = a bond, -O-, -NH- or -CH2-, provided that only one of X, Y and Z can be a bond at any one time and provided that X and Y do not both simultaneously = -O- or -C(O)-. N = 0-2; each R2 = halogen or C1-C6 alkyl; q = 0-1; R3 = -NHC(O)R10, -C(O)NR11R12 or -COOR12a; R4, R5, R6, R7 and R8 = H or a C1-C6 alkyl group; t = 0-2; each R9 = halogen, cyano, hydroxy, carboxy, C1-C6 alkoxy, C1-C6 alkoxycarbonyl, C1-C6 haloalkyl, or

C1-C6 alkyl; addnl. details are given in the claims. Methods of preparation are claimed and >200 example prepns. are included. For example, II was prepared in 2 steps starting from N-(2-hydroxyphenyl)acetamide, ((2S)-oxiran-2-yl)methyl and Cs2CO3 in DMF to give N-[2-[((2S)-oxiran-2-yl)methoxy]phenyl]acetamide as an intermediate, which was reacted with 5-chloro-3H-spiro[1-benzofuran-2,4'-piperidine] in EtOH to give II.

IT 644968-87-6P 644969-01-7P 644969-11-9P
644969-20-0P 644969-46-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of tricyclic spiropiperidines or spiropyrrolidines useful against disorders affected by modulation of chemokine receptors)

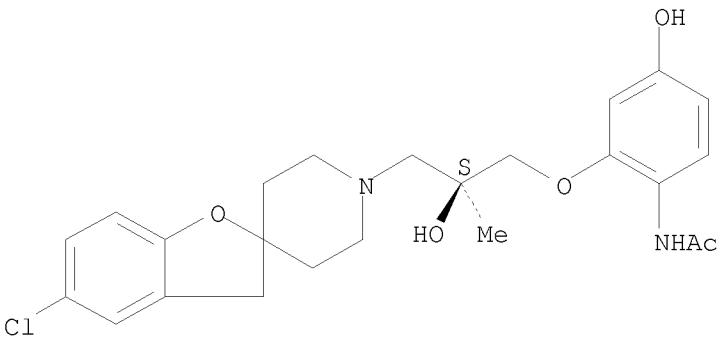
RN 644968-87-6 CAPLUS

CN Acetamide, N-[2-[(2S)-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)-2-hydroxy-2-methylpropoxy]-4-hydroxyphenyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

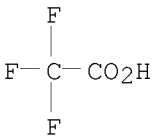
CRN 644968-86-5
CMF C24 H29 Cl N2 O5

Absolute stereochemistry.



CM 2

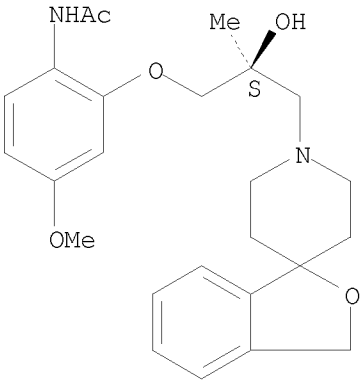
CRN 76-05-1
CMF C2 H F3 O2



RN 644969-01-7 CAPLUS

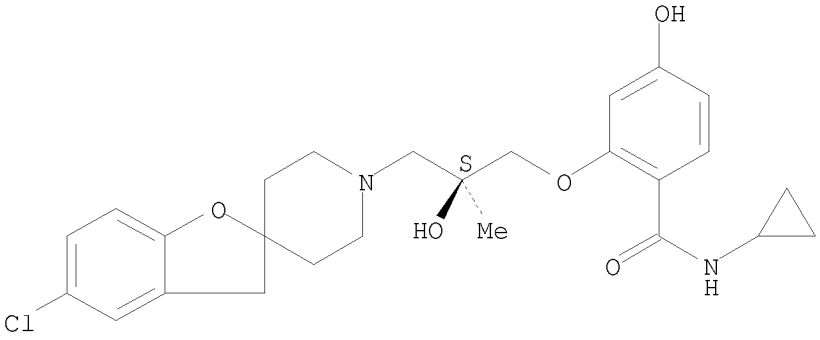
CN Acetamide, N-[2-[(2S)-2-hydroxy-2-methyl-3-(spiro[isobenzofuran-1(3H),4'-piperidin]-1'-yl)propoxy]-4-methoxyphenyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 644969-11-9 CAPLUS
CN Benzamide, 2-[(2S)-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)-2-hydroxy-2-methylpropoxy]-N-cyclopropyl-4-hydroxy- (CA INDEX NAME)

Absolute stereochemistry.

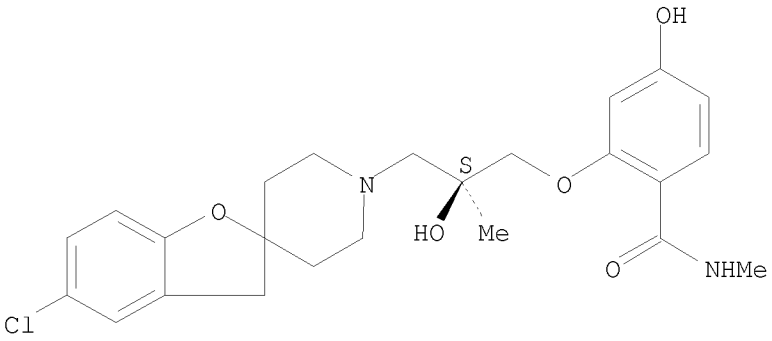


RN 644969-20-0 CAPLUS
CN Benzamide, 2-[(2S)-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)-2-hydroxy-2-methylpropoxy]-4-hydroxy-N-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

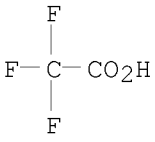
CRN 644969-19-7
CMF C24 H29 Cl N2 O5

Absolute stereochemistry.



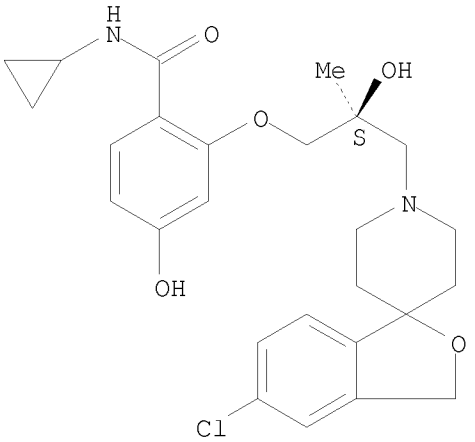
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 644969-46-0 CAPLUS
CN Benzamide, 2-[(2S)-3-(5-chlorospiro[isobenzofuran-1(3H),4'-piperidin]-1'-yl)-2-hydroxy-2-methylpropoxy]-N-cyclopropyl-4-hydroxy- (CA INDEX NAME)

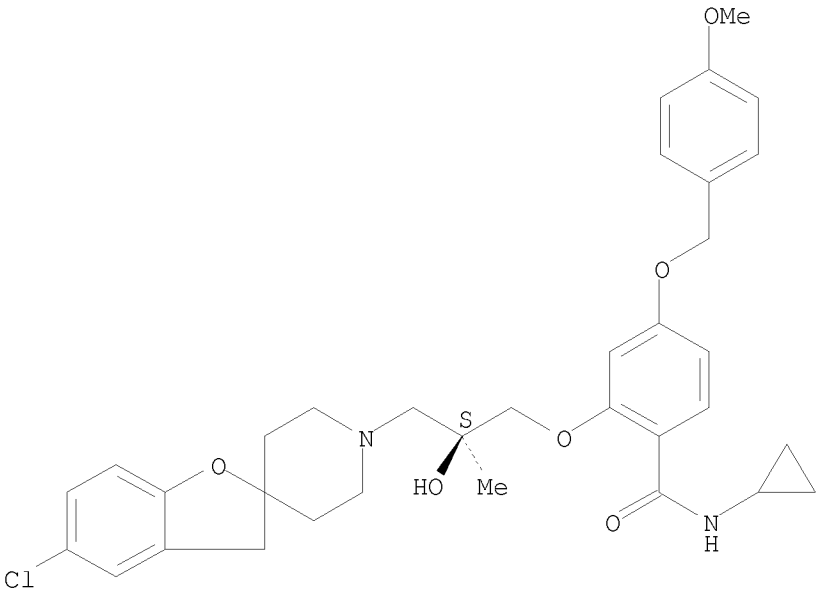
Absolute stereochemistry.



IT 644969-14-2P 644969-23-3P 644969-47-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tricyclic spiropiperidines or spiropyrrolidines useful against disorders affected by modulation of chemokine receptors)
RN 644969-14-2 CAPLUS
CN Benzamide, 2-[(2S)-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)-

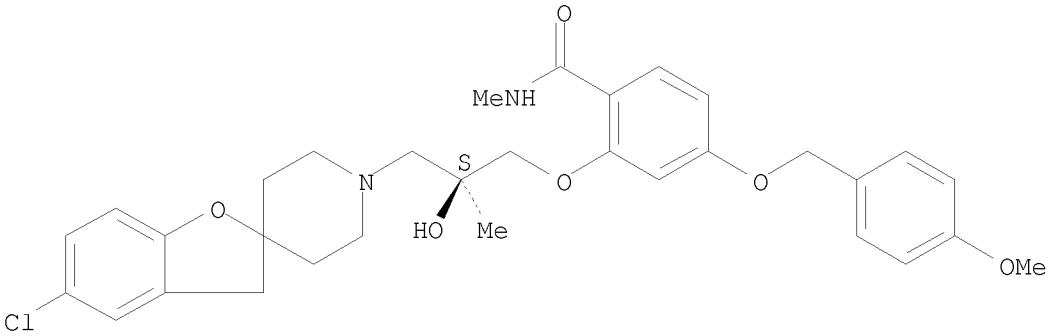
2-hydroxy-2-methylpropoxy]-N-cyclopropyl-4-[(4-methoxyphenyl)methoxy]-
(CA INDEX NAME)

Absolute stereochemistry.



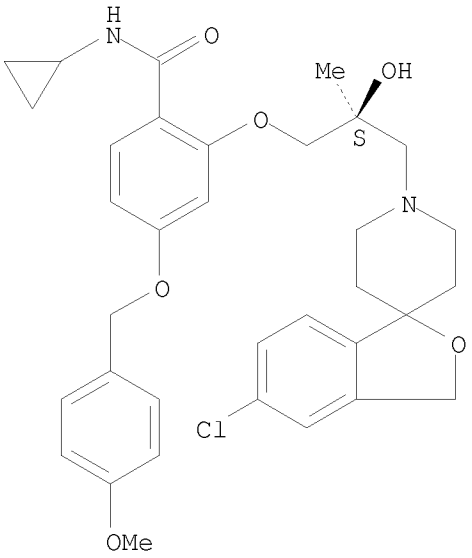
RN 644969-23-3 CAPLUS
CN Benzamide, 2-[(2S)-3-(5-chlorospiro[benzofuran-2(3H),4'-piperidin]-1'-yl)-
2-hydroxy-2-methylpropoxy]-4-[(4-methoxyphenyl)methoxy]-N-methyl- (CA
INDEX NAME)

Absolute stereochemistry.



RN 644969-47-1 CAPLUS
CN Benzamide, 2-[(2S)-3-(5-chlorospiro[isobenzofuran-1(3H),4'-piperidin]-1'-
yl)-2-hydroxy-2-methylpropoxy]-N-cyclopropyl-4-[(4-methoxyphenyl)methoxy]-
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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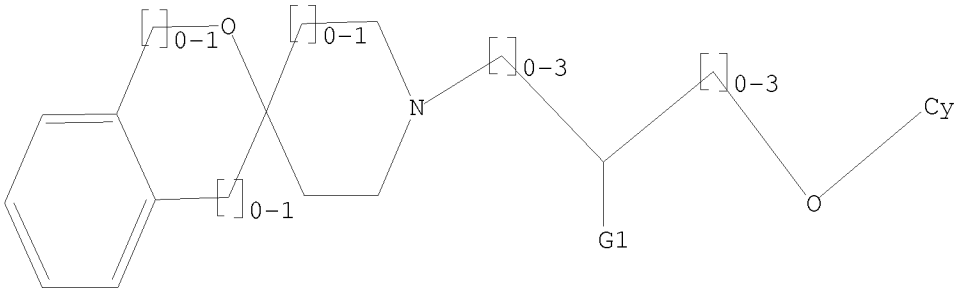
FILE 'REGISTRY' ENTERED AT 13:42:32 ON 12 DEC 2008
L1 STRUCTURE UPLOADED
L2 3 S L1
L3 74 S L1 FULL

FILE 'CAPLUS' ENTERED AT 13:43:02 ON 12 DEC 2008
L4 6 S L3

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 C,N,X

Structure attributes must be viewed using STN Express query preparation.

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